

**Amendments to the claims:**

*This listing of claims replaces all prior versions and listings of claims in the application.*

1. (currently amended) A method of treating acne in a human in need thereof comprising administering orally or intravenously to said human a non-antibiotic tetracycline compound, or a pharmaceutically acceptable salt thereof, in a sub-antibacterial an amount that reduces lesion count, without administering a bisphosphonate compound.

2. (original) A method according to Claim 1, wherein said acne is acne vulgaris, cystic acne, acne atrophica, bromide acne, chlorine acne, acne conglobata, acne cosmetica, acne detergentians, epidemic acne, acne estivalis, acne fulminans, halogen acne, acne indurata, iodide acne, acne keloid, acne mechanica, acne papulosa, pomade acne, premenstrual acne, acne pustulosa, acne rosacea, acne scorbutica, acne scrofulosorum, acne urticata, acne varioliformis, acne venenata, propionic acne, acne excoeciae, gram negative acne, steroid acne, or nodulocystic acne.

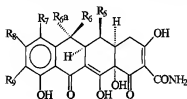
Claims 3-23 (cancelled).

24. (currently amended) A method of treating acne in a human in need thereof comprising administering orally or intravenously to said human a non-antibiotic tetracycline compound according to Claim 23, wherein said non-antibiotic tetracycline compound is:

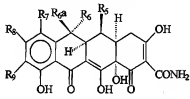
- 4-de(dimethylamino)tetracycline (CMT-1),
- tetracyclinonitrile (CMT-2),
- 6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline (CMT-3),
- 4-de(dimethylamino)-7-chlorotetracycline (CMT-4),
- tetracycline pyrazole (CMT-5)
- 4-hydroxy-4-de(dimethylamino)tetracycline (CMT-6),
- 4-de(dimethylamino)-12 $\alpha$ -deoxytetracycline (CMT-7),
- 6- $\alpha$ -deoxy-5-hydroxy-4-de(dimethylamino)tetracycline (CMT-8),
- 4-de(dimethylamino)-12 $\alpha$ -deoxyanhydrotetracycline (CMT-9), or

4-de(dimethylamino)minocycline (CMT-10) or  
a pharmaceutically acceptable salt of any such compound.

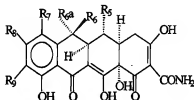
25. (currently amended) A method according to ~~Claim 1~~ Claim 23, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:



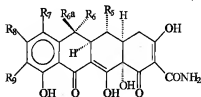
Structure C



Structure D



Structure E



Structure F

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, diazonium, di(lower alkyl)amino and  $\text{RCH}(\text{NH}_2)\text{CO}$ ;

R is hydrogen or lower alkyl; and  
pharmaceutically acceptable salts of any such compound thereof, with the following provisos:

when either R7 and R9 are hydrogen then R8 must be halogen; and

when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro, halogen, dimethylamino or diethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and

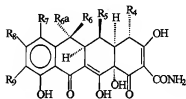
when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8 must be halogen; and

when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

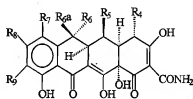
when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen.

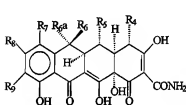
26. (currently amended) A method according to Claim 1 Claim-23, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:



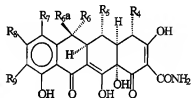
Structure G



Structure H



Structure I



Structure J

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, and di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R4 is selected from the group consisting of NOH, N-NH-A, and NH-A,  
 where A is a lower alkyl group;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, di(lower alkyl)amino and  $RCH(NH_2)CO$ ;

R is hydrogen or lower alkyl; and  
pharmaceutically acceptable salts of any such compound thereof; with the following provisos:

when R4 is NOH, N-NH-alkyl or NH-alkyl and R7, R6-a, R6, R5, and R9 are all hydrogen, then R8 must be halogen; and

when R4 is NOH, R6-a is methyl, R6 is hydrogen or hydroxyl, R7 is halogen, R5 and R9 are both hydrogen, then R8 must be halogen; and

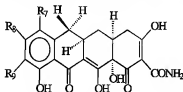
when R4 is N-NH-alkyl, R6-a is methyl, R6 is hydroxyl and R7, R5, R9 are all hydrogen, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a, R6, R5 and R9 are all hydrogen, R7 is hydrogen, amino, mono(lower alkyl)amino, halogen, di(lower alkyl)amino or hydroxyl, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is mono(lower alkyl)amino or di(lower alkyl)amino, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a is methyl, R6 is hydroxy or hydrogen and R7, R5, and R9 are all be hydrogen, then R8 must be halogen.

27. (currently amended) A method according to Claim 1 ~~Claim~~-23 wherein the non-antibiotic tetracycline compound is selected from the group consisting of:

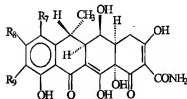


Structure K

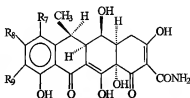
wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	acylamino
dimethylamino	hydrogen	diazonium
dimethylamino	chloro	amino
hydrogen	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
monoalkylamino	chloro	amino
nitro	chloro	amino
dimethylamino	chloro	acylamino
dimethylamino	chloro	dimethylamino
hydrogen	hydrogen	dimethylamino
dimethylamino	hydrogen	hydrogen

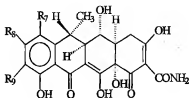
and



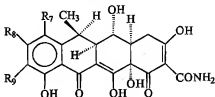
Structure L



Structure M



Structure N



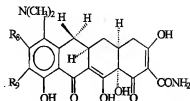
Structure O

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	acylamino
hydrogen	hydrogen	diazonium
hydrogen	hydrogen	dimethylamino
diazonium	hydrogen	hydrogen
ethoxythiocarbonylthio	hydrogen	hydrogen
dimethylamino	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
hydrogen	chloro	amino
amino	chloro	hydrogen

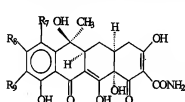
acylamino	chloro	hydrogen
monoalkylamino	chloro	amino
nitro	chloro	amino

and

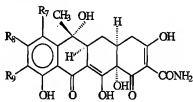


Structure P

wherein: R8 is hydrogen or halogen and R9 is selected from the group consisting of nitro, (N,N-dimethyl)glycylamino, and ethoxythiocarbonylthio; and



Structure Q



Structure R

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

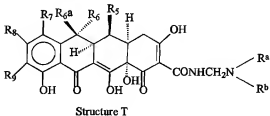
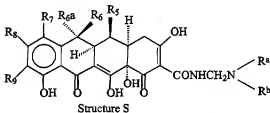
R7	R8	R9
amino	hydrogen	hydrogen
nitro	hydrogen	hydrogen
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
bromo	hydrogen	hydrogen
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro

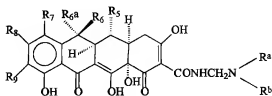


hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
diethylamino	hydrogen	hydrogen
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	methylamino
dimethylamino	hydrogen	acylamino
dimethylamino	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
hydrogen	chloro	amino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
monoalkylamino	chloro	amino
nitro	chloro	amino

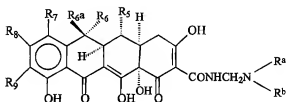
and pharmaceutically acceptable salts of any such compound thereof.

28. (currently amended) A method according to Claim 1 ~~Claim 23~~, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:

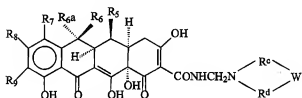




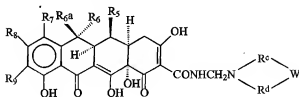
Structure U



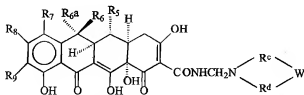
Structure V



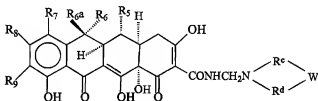
Structure W



Structure X



Structure Y



Structure Z

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, diazonium, di(lower alkyl)amino and  $RCH(NH_2)CO$ ;

R is hydrogen or lower alkyl;

R<sup>a</sup> and R<sup>b</sup> are selected from the group consisting of hydrogen, methyl, ethyl, n-propyl and 1-methylethyl with the proviso that R<sup>a</sup> and R<sup>b</sup> cannot both be hydrogen;

R<sup>c</sup> and R<sup>d</sup> are, independently,  $(CH_2)_nCHR^e$  wherein n is 0 or 1 and R<sup>e</sup> is selected from the group consisting of hydrogen, alkyl, hydroxy, lower(C<sub>1</sub>-C<sub>3</sub>) alkoxy, amino, or nitro; and,

W is selected from the group consisting of  $(\text{CHR}^*)_m$  wherein m is 0-3 and said  $\text{R}^*$  is as above,  $\text{NH}$ ,  $\text{N}(\text{C}_1\text{-C}_3)$  straight chained or branched alkyl, O, S and  $\text{N}(\text{C}_1\text{-C}_4)$  straight chain or branched alkoxy; and,

pharmaceutically acceptable salts of any such compound thereof.

29. (currently amended) A method according to Claim 1 Claim 23, wherein the non-antibiotic tetracycline compound selected from the group consisting of structures S-Z has the following provisos:

when either R7 and R9 are hydrogen then R8 must be halogen; and

when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro, halogen, dimethylamino or diethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and

when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8 must be halogen; and

when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

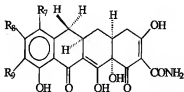
when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen

and a pharmaceutically acceptable salt of any such compound.

Claims 30 - 31 (cancelled).

32. (currently amended) A method according to Claim 1 ~~Claim 23~~, wherein said tetracycline compound has a general formula:

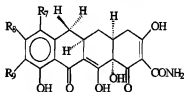


Structure K

wherein R7, R8, and R9 taken together are, respectively, hydrogen, hydrogen and dimethylamino or a pharmaceutically acceptable salt of any such compound.

Claim 33 (canceled).

34. (currently amended) A method according to Claim 1 ~~Claim 23~~, wherein said tetracycline compound is selected from the group consisting of:

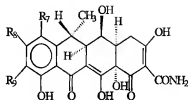


Structure K

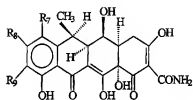
wherein R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
hydrogen	hydrogen	amino
hydrogen	hydrogen	palmitamide

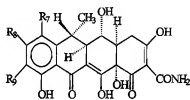
and



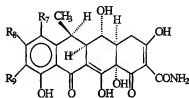
Structure L



Structure M



Structure N



Structure O

wherein R7, R8, and R9 taken together in each case, have the following meanings:

R7

hydrogen  
 hydrogen  
 hydrogen  
 hydrogen

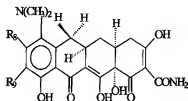
R8

hydrogen  
 hydrogen  
 hydrogen  
 hydrogen

R9

acetamido  
 dimethylaminoacetamido  
 nitro  
 amino

and



Structure P

wherein R<sub>8</sub>, and R<sub>9</sub> taken together are, respectively, hydrogen and nitro and a pharmaceutically acceptable salt of any such compound.

Claim 35 (canceled).

36. (currently amended) A method of treating acne in a human in need thereof comprising systemically administering to said human an effective amount of 6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline without administering a bisphosphonate compound.

Claim 37 (cancelled).

38. (currently amended) A method according to Claim 36, wherein said administration is systemic oral administration.

Claims 39 - 64 (cancelled).

65. (new) A method according to Claim 36, wherein the human has skin lesions associated with the acne, and the method reduces the skin lesion count.

66. (new) A method according to Claim 65, wherein the lesions are pustules, papules, cysts, nodules, or comedones.

67. (new) A method according to Claim 65, wherein the lesions are pustules and papules.

68. (new) A method according to Claim 65, wherein the lesions are comedones.
69. (new) A method according to Claim 65, wherein the acne is acne rosacea.
70. (new) A method according to Claim 67, wherein the acne is acne vulgaris.
71. (new) A method according to Claim 69 or Claim 70, wherein said 6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline is administered by sustained release.
72. (new) A method according to Claim 69 or Claim 70, wherein said 6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline is administered once a day.
73. (new) A method according to Claim 69 or Claim 70, wherein the amount is an amount that results in no reduction of skin microflora during a six-month treatment.
74. (new) A method of treating acne in a human in need thereof comprising administering orally or intravenously to said human a tetracycline compound, or a pharmaceutically acceptable salt thereof, in an amount that reduces lesion count, without administering a bisphosphonate compound, wherein a substituent at any of positions 1-4 and 10-12 of said tetracycline compound or said pharmaceutically acceptable salt thereof has been replaced, and wherein the resulting compound or salt has substantially less or effectively no antibiotic activity.
75. (new) A method according to claim 74, wherein the tetracycline compound is 6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline.
76. (new) A method of treating acne in a human in need thereof, the method comprising administering orally or intravenously to said human a pharmaceutical preparation comprising 6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline, which pharmaceutical preparation does not also comprise a bisphosphonate compound.



77. (new) A method of reducing lesions associated with acne in a human in need thereof, the method comprising orally administering to said human an effective amount of 6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline, the method not comprising administering a bisphosphonate compound.